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Patient Health Questionnaire-9 scores do not accurately estimate depression prevalence: individual participant data meta-analysis

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ABSTRACT

Objective: Depression symptom questionnaires are not for diagnostic classification. Patient Health Questionnaire-9 (PHQ-9) scores ≥ 10 are nonetheless often used to estimate depression prevalence. We compared PHQ-9 ≥ 10 prevalence to Structured Clinical Interview for DSM (SCID) major depression prevalence and assessed whether an alternative PHQ-9 cutoff could more accurately estimate prevalence.

Study design and setting: Individual participant data meta-analysis of datasets comparing PHQ-9 scores to SCID major depression status.

Results: 9,242 participants (1,389 SCID major depression cases) from 44 primary studies were included. Pooled PHQ-9 ≥ 10 prevalence was 24.6% (95% CI: 20.8%, 28.9%); pooled SCID major depression prevalence was 12.1% (95% CI: 9.6%, 15.2%); pooled difference was 11.9% (95% CI: 9.3%, 14.6%). Mean study-level PHQ-9 ≥ 10 to SCID-based prevalence ratio was 2.5 times. PHQ-9 ≥ 14 and the PHQ-9 diagnostic algorithm provided prevalence closest to SCID major depression prevalence, but study-level prevalence differed from SCID-based prevalence by an average absolute difference of 4.8% for PHQ-9 ≥ 14 (95% prediction interval: -13.6%, 14.5%) and 5.6 % for the PHQ-9 diagnostic algorithm (95% prediction interval: -16.4%, 15.0%).

Conclusion: PHQ-9 ≥ 10 substantially overestimates depression prevalence. There is too much heterogeneity to correct statistically in individual studies.

Key words: depression prevalence, PHQ-9, SCID, individual participant data meta-analysis

Running title: Depression prevalence based on PHQ-9 vs. SCID

HIGHLIGHTS

- We compared Patient Health Questionnaire-9 (PHQ-9) ≥ 10 prevalence to Structured Clinical Interview for DSM (SCID) major depression prevalence in 44 primary studies (9,242 participants, 1,389 SCID major depression cases) that administered the PHQ-9 and SCID.
- We also examined whether an alternative PHQ-9 cutoff could more accurately estimate prevalence.
- Pooled PHQ-9 ≥ 10 prevalence (25%) was double pooled SCID major depression prevalence (12%); pooled difference from each study was 12%.
- PHQ-9 ≥ 14 and PHQ-9 diagnostic algorithm prevalence most closely matched SCID major depression prevalence, but study-level PHQ-9 ≥ 14 and PHQ-9 diagnostic algorithm prevalence differed from SCID major depression prevalence with 95% prediction intervals of -14% to 15% and -16% to 15%, respectively.
- Estimates of depression prevalence should be based on validated diagnostic interviews designed for determining case status; users should evaluate published reports of depression prevalence to ensure that they are based on methods intended to classify major depression.

1. INTRODUCTION

Disease prevalence estimates have important implications for interpreting medical research, understanding disease burden, and making decisions about healthcare resource utilization.[1] In mental health research, major depression classification requires using validated diagnostic interviews.[2,3] Administering diagnostic interviews in large enough samples to estimate prevalence, however, is resource intensive. Thus, researchers sometimes use self-report depression symptom questionnaires, or screening tools, instead, and label the percentage of participants scoring above a screening cutoff as depression prevalence.[4,5] A 2018 study identified 19 primary studies listed in PubMed in a 3-month period whose titles indicated that they assessed prevalence of depression or depressive disorders and found that 89% were based on screening questionnaires only.[4]

Some self-report questionnaires include the same symptoms evaluated in validated diagnostic interviews. None, however, include all components of diagnostic interviews, such as assessment of functional impairment or investigation of non-psychiatric medical conditions that can cause similar symptoms.[4] Using depression symptom questionnaires and cutoffs intended for screening to assess depression prevalence may overestimate prevalence. This is because screening attempts to identify previously unrecognized cases; cutoffs are set to cast a wide net and identify many more patients who may have depression than meet diagnostic criteria.

A recent review examined meta-analyses of depression prevalence published in 2008-2017.[5] Of 81 prevalence estimates reported in abstracts of 69 meta-analyses, 10% were based on diagnostic interviews, 44% were based on screening or rating tools, and 46% combined results from diagnostic interviews and screening or rating tools. Mean reported prevalence was 31% among meta-analyses based on screening or rating tools compared to 17% with diagnostic

interviews.[5] The degree to which screening tools exaggerate prevalence, however, depends on the screening tool and cutoff used.[4,5]

We do not know of any studies that have evaluated the degree to which specific screening tool and cutoff combinations overestimate depression prevalence.[4,5] The Patient Health Questionnaire-9 (PHQ-9)[6-8] is the most commonly used depression screening tool in primary care.[9] Its nine items align with the Diagnostic and Statistical Manual of Mental Disorders (DSM) criteria for major depressive episode.[10-12] The standard cutoff, ≥ 10, is well-established for screening to detect major depression and maximized combined sensitivity and specificity in a recent individual participant data meta-analysis (IPDMA).[6-8,13] PHQ-9 ≥ 10 has been used to estimate depression prevalence in primary research studies and via synthesis in meta-analyses, including in very high-impact journals.[14-16] It is also sometimes used to diagnose depression and make treatment decisions for individual patients.[6,17-19]

Our objective was to use an IPDMA approach to (1) compare PHQ-9 ≥ 10 prevalence to major depression prevalence based on a well-validated semi-structured diagnostic interview, the Structured Clinical Interview for DSM (SCID);[20] and (2) use a prevalence matching approach[4,21] to determine if a PHQ-9 cutoff could be set to match SCID-based prevalence with sufficiently low heterogeneity to accurately estimate prevalence in individual studies.

2. METHODS

This study used a subset of data accrued for an IPDMA of the accuracy of the PHQ-9 for screening to detect major depression.[13] Detailed methods were registered in PROSPERO (CRD42014010673), and a protocol was published.[22] This analysis was not part of the original IPDMA protocol.

2.1 Study Selection

In the main IPDMA, datasets from articles in any language were eligible for inclusion if (1) they included PHQ-9 scores; (2) they included diagnostic classifications for current Major Depressive Episode (MDE) or Major Depressive Disorder (MDD) based on DSM[10-12] or International Classification of Diseases[23] criteria, using a validated semi-structured or fully structured interview; (3) the PHQ-9 and diagnostic interview were administered within two weeks of each other; (4) participants were ≥18 years and not recruited from youth or school-based settings; and (5) participants were not recruited from psychiatric settings or because they were identified as having depressive symptoms. Datasets where not all participants were eligible were included if primary data allowed selection of eligible participants.

For the present study, we included primary studies that based diagnoses on the SCID.[20] The SCID is a semi-structured diagnostic interview intended to be conducted by an experienced diagnostician; it requires clinical judgment and allows rephrasing questions and probes. The reason for including only SCID studies is that in analyses using large IPDMA databases,[24-26] we found that, compared to semi-structured interviews, fully structured interviews, which are designed for administration by lay interviewers, identify more participants with low-level symptoms as depressed but fewer participants with high-level symptoms. These results were consistent with the idea that semi-structured interviews most closely replicate clinical interviews done by trained professionals, whereas fully structured interviews are less resource-intensive options that can be administered by research staff without diagnostic skills but may misclassify major depression in many participants. In our PHQ-9 IPDMA database, 44 of 47 studies that used semi-structured interviews used the SCID. Thus, to reduce heterogeneity, we only included these 44 studies in main analyses.

In sensitivity analyses, we also included the three studies that used other semi-structured interviews. We considered also incorporating published results from eligible studies that did not contribute data to the IPDMA. However, only 3 of 14 such studies[27-29] (970 participants, 77 major depression cases) reported sufficient information to compare PHQ-9 ≥ 10 and SCID-based prevalence, and these studies did not report information necessary to be included in all prevalence matching analyses.

2.2 Data Sources and Searches

A medical librarian searched Medline, Medline In-Process & Other Non-Indexed Citations via Ovid, PsycINFO, and Web of Science from January 1 2000-May 9 2018, using a peer-reviewed[30] search strategy (Supplementary Material: Appendix Methods). We also reviewed reference lists of relevant reviews and queried contributing authors about non-published studies.

Two investigators independently reviewed titles and abstracts for eligibility. If either deemed a study potentially eligible, the full-text was reviewed by two investigators, independently, with disagreements resolved by consensus, consulting a third investigator when necessary.

2.3 Data Contribution and Synthesis

Authors of eligible datasets were invited to contribute de-identified primary data, including PHQ-9 scores and major depression classification status. We emailed corresponding authors of eligible studies at least three times, as necessary. If no response, we emailed co-authors and attempted phone contact.

Prior to integrating individual datasets into our synthesized dataset, we compared published participant characteristics and diagnostic accuracy results with results from raw datasets and resolved discrepancies with the original investigators. When datasets included statistical weights to

reflect sampling procedures, we used provided weights. For studies where sampling procedures merited weighting, but the original study did not weight, we constructed weights using inverse selection probabilities.

2.4 Data Analysis

Comparison of PHQ-9 ≥ 10 Prevalence and SCID Major Depression Prevalence

For each primary study, we estimated the percentage of participants who scored ≥ 10 on the PHQ-9, the percentage of participants classified as having major depression based on the SCID, the difference of these percentages, and the ratio. Then, across studies, we pooled prevalence for PHQ-9 ≥ 10, prevalence for the SCID, and differences in prevalence.

Prevalence Matching

To identify which PHQ-9 scoring approach best matched SCID-based prevalence, we estimated pooled differences in prevalence for each possible PHQ-9 cutoff and the PHQ-9 diagnostic algorithm compared to SCID. The scoring approach with the smallest pooled difference was chosen to be the "prevalence match scoring approach." Then, for each included study, we estimated the difference and ratio in prevalence for the prevalence match scoring approach versus SCID. We determined the mean and median absolute difference and range of differences across all studies. To illustrate the range of difference values that would be expected if a new study were to compare prevalence based on the prevalence match scoring approach to prevalence based on SCID, we estimated 95% prediction intervals for the differences. For the diagnostic algorithm, which requires five or more items with scores of ≥ 2 points, with at least one being depressed mood or anhedonia,[8] three studies[31-33] (524 participants) and 88 additional participants from other studies (612 participants total, 7%) were excluded, as they did not provide PHQ-9 item scores, which are necessary to determine diagnostic algorithm criteria. In

sensitivity analyses, we evaluated if results differed if the 612 participants were excluded from all analyses rather than just those involving the diagnostic algorithm.

All meta-analyses incorporated sampling weights and were conducted in R (R version 3.4.1; R Studio version 1.0.143) using the lme4 package. To estimate pooled prevalence values, generalized linear mixed-effects models with a logit link function were fit using the glmer function. To estimate pooled difference values, linear mixed-effects models were fit using the lmer function. To account for correlation between subjects within the same primary study, random intercepts were fit for each primary study. To quantify heterogeneity, we reported the estimated between-study variance (τ^2) for each analysis.

In post-hoc analyses, we investigated whether differences in prevalence for the PHQ-9 prevalence match scoring approach and SCID were associated with study and participant characteristics. To do this, we fit additional linear mixed-effects models for pooled prevalence difference, including age, sex, country human development index ("very high", "high", or "low-medium", based on the United Nation's 2018 Human Development Index) and recruitment setting category (primary care, nonmedical care, inpatient specialty care, or outpatient specialty care) as fixed-effect covariates. For these analyses, we excluded 56 participants (<1%) missing age or sex data.

3. RESULTS

3.1 Search Results and Inclusion of Primary Study Datasets

Of 9,674 unique titles and abstracts identified from the database search for the main IPDMA, 9,198 were excluded after title and abstract review and 297 after full-text review, leaving 179 eligible articles with data from 123 unique participant samples, of which 95 (77.2%) contributed datasets. Authors of included studies contributed data from five unpublished studies,

for a total of 100 datasets. Of these, for the present study's main analyses, we excluded 56 studies that classified major depression using a diagnostic interview other than the SCID (Figure 1). Thus, the main analyses of the present study included 9,242 participants (1,389 major depression cases) from 44 primary studies.[31-72] Among the 28 eligible primary studies that did not provide datasets for the main IPDMA, 14 used the SCID (4,408 participants). Thus, the main analyses included 75.9% of eligible studies that used the SCID (44 of 58) and 67.7% of eligible participants (9,242 of 13,650). Table 1 shows the characteristics of each included study.

In sensitivity analyses, we included data from three additional studies (1,992 participants; 139 major depression cases) that provided individual participant data but administered a semi-structured interview other than the SCID (Table 1)[73-75].

3.2 Comparison of PHQ-9 ≥ 10 Prevalence and SCID Major Depression Prevalence

The percentage of participants with PHQ-9 ≥ 10 in each of the 44 SCID studies ranged from 5.3% to 64.8%; pooled prevalence was 24.6% (95% confidence interval [CI]: 20.8%, 28.9%; τ^2: 0.505). The percentage of participants with SCID major depression ranged from 0.6% to 56.4%; pooled prevalence was 12.1% (95% CI: 9.6%, 15.2%; τ^2: 0.703).

Differences in prevalence (PHQ-9 ≥ 10 minus SCID) ranged from -6.0% to 46.9%. The pooled difference was 11.9% (95% CI: 9.3%, 14.6%; τ^2: 0.007).

The ratio of PHQ-9 ≥ 10 prevalence to SCID-based prevalence ranged from 0.7 to 10.0 times (mean: 2.5; median: 1.9). The mean ratio was 3.8 times for the 17 studies with SCID-based prevalence < 10% (mean difference: 13.3%), 2.0 times for the 16 studies with SCID-based prevalence between 10% and 20% (mean difference: 12.7%), and 1.3 times for the 11 studies with SCID-based prevalence of ≥ 20% (mean difference: 8.9%).

3.3 Prevalence Matching

PHQ-9 ≥ 14 (pooled difference in prevalence: 0.5%, 95% CI: -1.7%, 2.6%, τ^2: 0.005) and the PHQ-9 diagnostic algorithm (pooled difference in prevalence: -0.7%, 95% CI: -3.2%, 1.8%; τ^2: 0.006) provided prevalence closest to SCID-based prevalence. Pooled differences in prevalence for PHQ-9 ≥ 13 and ≥ 15 compared to SCID were 2.6% and -2.0%.

In the 44 individual SCID studies, differences between the percentage of participants with PHQ-9 ≥ 14 and SCID major depression ranged from -18.7% to 29.7% (mean absolute difference: 4.8%). Of 44 prevalence estimates based on PHQ-9 ≥ 14, 24 (54.5%) were ≤ 0.75 times or ≥ 1.25 times the SCID-based prevalence. The 95% prediction interval for the difference in prevalence was -13.6% to 14.5%. For the PHQ-9 diagnostic algorithm, study-level differences in prevalence ranged from -20.1% to 27.1% (mean absolute difference: 5.6%). Of 41 prevalence estimates based on the PHQ-9 diagnostic algorithm, 28 (68.3%) were ≤ 0.75 times or ≥ 1.25 times the SCID-based prevalence. The 95% prediction interval for the difference in prevalence was -16.4% to 15.0%. No study or participant characteristics were significantly associated with differences in prevalence for either of the PHQ-9 prevalence match scoring approaches compared to SCID.

3.4 Sensitivity Analyses

Results for all analyses were similar when data from the three studies with semi-structured interviews other than the SCID were added or when the 612 participants without data to determine PHQ-9 diagnostic algorithm classification were excluded.

4. DISCUSSION

Primary studies and meta-analyses that describe their results as reflecting prevalence of depression or depressive disorders are frequently based on depression screening tools, which are not designed for this purpose, rather than validated diagnostic interviews.[4,5] The PHQ-9 is often

used to generate what are described by researchers as depression prevalence estimates. The present study found that using PHQ-9 ≥ 10 to assess depression prevalence, which is commonly done, overestimated depression prevalence compared to prevalence based on actual diagnostic criteria by 11.9% (mean ratio: 2.5 times).

These results are consistent with what was predicted in a previous analysis that used hypothetical estimates of sensitivity and specificity to demonstrate how depression screening tools would be expected to inflate prevalence.[4] Results are also consistent with the findings of a meta-research review of prevalence estimates from 69 meta-analyses that found higher mean depression prevalence based on screening or rating tools than based on diagnostic interviews.[5] Thus, if a screening tool, such as the PHQ-9 ≥ 10, is used to estimate prevalence, prevalence will appear to be substantial in virtually all populations, even when true prevalence is very low. This could have important ramifications in terms of policies, service planning and healthcare budgets.

Identifying a PHQ-9 cutoff that could be used to match true prevalence based on a diagnostic interview would allow researchers to use inexpensive questionnaires instead of more costly interview methods for prevalence estimation. We tested a prevalence matching approach and found that PHQ-9 ≥ 14 and the PHQ-9 diagnostic algorithm provided the smallest differences in prevalence compared to SCID major depression, but heterogeneity was high and not associated with study or participant characteristics. The mean absolute difference between prevalence based on PHQ-9 versus SCID in individual studies was 4.8% for PHQ-9 ≥ 14 and 5.6% for the PHQ-9 diagnostic algorithm, reflecting both overestimation and underestimation. For more than half of the studies examined, PHQ-9 ≥ 14 prevalence was less than 75% or more than 125% of SCID-based prevalence; for the PHQ-9 diagnostic algorithm the fraction was over two-thirds. The 95% prediction interval for the difference between PHQ-9 ≥ 14 and SCID-based

prevalence ranged from 14% below to 15% above SCID-based prevalence; for the PHQ-9 diagnostic algorithm it was from 16% below to 15% above SCID-based prevalence.

Researchers sometimes report prevalence estimates based on cutoffs from questionnaires, including the PHQ-9, as prevalence of "clinically significant" symptoms or "symptoms" of depression, rather than "depression".[14,76,77] However, screening tool cutoffs do not reflect a meaningful divide between impairment and non-impairment. Patients scoring at or above virtually any cutoff would be expected to have greater impairment than patients scoring below the cutoff, but no evidence has established any single cutoff for establishing an impairment threshold or that would support clinical decision-making for individual patients without a validated clinical assessment.[4]

Research on screening using the PHQ-9 would be expected to report the proportion of patients who score at or above screening cutoffs because this provides information on the number of patients who would need resources for further mental health assessment. Reporting this percentage as depression prevalence, however, would be akin, for example, to reporting the proportion of women with positive mammogram screens as the prevalence of breast cancer and, as shown in the present study, would dramatically overestimate prevalence.

This is the first study to estimate the degree to which using PHQ-9 $\geq$ 10 to estimate depression prevalence, a common practice, leads to overestimation of prevalence. Strengths of the study are that we incorporated data from 44 primary studies and that we directly compared PHQ-9 $\geq$ 10 prevalence estimates to those based on the SCID, a rigorous semi-structured interview intended to facilitate the standardized application of actual diagnostic criteria by trained diagnosticians.[10-12] This study had some limitations. First, we were unable to include data from 14 of 58 published eligible datasets (24%). Second, included datasets were almost

exclusively from patients in healthcare settings where the presence of transdiagnostic somatic symptoms and adjustment to illness or injury may have contributed to error variance.[75] Third, included datasets were from a wide range of study settings, which may account for some of the observed heterogeneity. Fourth, overestimation of prevalence when screening tools are used is expected to be greater with lower true prevalence. This is because false positives are disproportionately high in low-prevalence populations and only minimally offset by false negative screens, which occur when true cases are missed by the screening test. However, we were unable to assess this because of the small number of heterogeneous datasets included. Fifth, not all SCID studies described interviewer qualifications; untrained interviewers may have reduced the ability to detect differences across interviews. Sixth, we only examined one depression screening tool, the PHQ-9, although we expect that other tools would similarly exaggerate depression prevalence.[4,5]

In summary, we found that using PHQ-9 ≥ 10 to estimate depression prevalence results in estimates that are, on average, 12% greater than what would be obtained using validated semi-structured diagnostic interviews. Substantial heterogeneity presents a barrier to using statistical methods to estimate major depression prevalence based on PHQ-9 ≥ 10 or based on any other PHQ-9 cutoff. Researchers should not report results from the PHQ-9 as prevalence of major depression. Users of evidence should evaluate reports of prevalence with caution and ensure that they are based on methods intended to classify major depression.

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5.2 Declaration of Competing Interests

All authors have completed the ICJME uniform disclosure form and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years with the following exceptions: Dr. Bernstein declares that he receives grants and personal fees from Abbvie, Janssen, Pfizer, and Takeda; grants from Shire Canada, Celgene, Boeringher Ingelheim, and

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5.3 Author Contributions

BLevis, ABenedetti, JPAI, JB, PC, SG, LAK, DM, SBP, IS, RCZ, and BDT were responsible for the study conception and design. JB and LAK designed and conducted database searches to identify eligible studies. SBP, SHA, DA, LA, HRB, ABeraldi, CNB, ABhana, CHB, GC, MHC, DC, KC, YC, CDQ, JRF, FHF, LG, LJG, EPG, CGG, BJH, EEH, KI, NJ, MEK, YK, MAL, SIL, SRL, BLöwe, RAM, LM, AM, KM, LN, FLO, IP, AP, SLP, TJQ, AGR, EHS, AS, LS, PLLT, MTR, AT, HCvW, PAV, LIW, JW and KW contributed primary datasets that were included in this study. BLevis, YS, ZN, CH, YW, AK, PMB, DN, MI, DBR, KER, NS, MA and BDT contributed to data extraction and coding for the individual participant data meta-analysis. BLevis, ABenedetti and BDT conducted analyses and interpreted results. BLevis and BDT drafted the manuscript. All authors provided a critical review and approved the final manuscript. BDT is the guarantor.

5.4 Data Sharing

Statistical codes and dataset used in the individual patient data meta-analysis can be requested from the corresponding author, Dr. Brett D. Thombs.

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Table 1. Characteristics of included studies and difference between percentage with PHQ-9 ≥ 10 and prevalence matching-based prevalence and prevalence based on diagnostic criteria for major depression

							PHQ-9 ≥ 10			Prevalence Matching					
Author, year	Country	Recruited Population	N Total	Mean (SD) Age	N (%) Female	N (%) Major Depression	N (%) PHQ-9 ≥ 10	% Difference: PHQ-9 ≥ 10 – Major Depression	Ratio: PHQ-9 ≥ 10 / Major Depression	N (%) PHQ-9 ≥ 14	% Difference: PHQ-9 ≥ 14 – Major Depression	Ratio: PHQ-9 ≥ 14 / Major Depression	N (%) PHQ-9 DA+	% Difference: PHQ-9 DA+ – Major Depression	Ratio: PHQ-9 DA+ / Major Depression
Studies from IPDMA that used the SCID and were Included in Main Analyses															
Alamri, 2017[a,31]	Saudi Arabia	Hospitalized elderly in medical and surgical wards	199	70 (8)	117 (59%)	24 (12.1%)	44 (22.1%)	10.1%	1.8	25 (12.6%)	0.5%	1.0	--	--	--
Amoozegar, 2017[34]	Canada	Migraine patients	203	43 (13)	41 (20%)	49 (24.1%)	72 (35.5%)	11.3%	1.5	40 (19.7%)	-4.4%	0.8	36 (17.7%)	-6.4%	0.7
Amtmann, 2015[b,35]	USA	Multiple sclerosis patients	164	55 (11)	127 (71%)	48 (17.6%)	90 (33.0%)	15.4%	1.9	55 (20.2%)	2.6%	1.1	42 (15.4%)	-2.2%	0.9
Ayalon, 2010[36]	Israel	Elderly primary care patients	151	76 (8)	61 (40%)	6 (4.0%)	14 (9.3%)	5.3%	2.3	7 (4.6%)	0.7%	1.2	6 (4.0%)	0.0%	1.0
Beraldi, 2014[c,37]	Germany	Cancer inpatients	116	52 (16)	37 (32%)	7 (6.0%)	21 (18.1%)	12.1%	3.0	4 (3.4%)	-2.6%	0.6	2 (1.7%)	-4.3%	0.3
Bernstein, 2018[38]	Canada	IBD patients	240	49 (15)	151 (63%)	21 (8.8%)	59 (24.6%)	15.8%	2.8	33 (13.8%)	5.0%	1.6	25 (10.4%)	1.7%	1.2
Bhana, 2015[39]	South Africa	Chronic care patients	679	47 (13)	509 (75%)	78 (11.5%)	53 (7.8%)	-3.7%	0.7	26 (3.8%)	-7.7%	0.3	15 (2.2%)	-9.3%	0.2
Bombardier, 2012[40]	USA	Inpatients with spinal cord injuries	160	42 (16)	36 (23%)	14 (8.8%)	43 (26.9%)	18.1%	3.1	23 (14.4%)	5.6%	1.6	17 (10.6%)	1.9%	1.2
Chagas, 2013[41]	Brazil	Outpatients with Parkinson's Disease	84	59 (12)	39 (46%)	19 (22.6%)	30 (35.7%)	13.1%	1.6	16 (19.0%)	-3.6%	0.8	12 (14.3%)	-8.3%	0.6
Chiabanda, 2016[d,42]	Zimbabwe	A primary care population with high HIV prevalence	264	38 (10)	208 (79%)	149 (56.4%)	171 (64.8%)	8.3%	1.1	122 (46.2%)	-10.2%	0.8	96 (36.4%)	-20.1%	0.6
Eack, 2006[43]	USA	Women seeking psychiatric services for their children at two mental health centers	48	39 (10)	48 (100%)	12 (25.0%)	24 (50.0%)	25.0%	2.0	17 (35.4%)	10.4%	1.4	17 (35.4%)	10.4%	1.4
Fann, 2005[a,b,e,32]	USA	Inpatients with traumatic brain injury	135	48 (20)	41 (28%)	45 (16.2%)	64 (22.5%)	6.3%	1.4	33 (12.2%)	-4.0%	0.8	--	--	--
Fiest, 2014[e,44]	Canada	Epilepsy outpatients	169	39 (15)	86 (51%)	23 (13.6%)	37 (21.9%)	8.3%	1.6	17 (10.1%)	-3.6%	0.7	17 (10.1%)	-3.6%	0.7
Fischer, 2014[f,45]	Germany	Heart failure patients	194	66 (11)	40 (21%)	11 (5.7%)	37 (19.1%)	13.4%	3.4	19 (9.8%)	4.1%	1.7	20 (10.3%)	4.6%	1.8
Gjerdingen, 2009 [f,46]	USA	Mothers registering their newborns for	419	30 (6)	419 (100%)	19 (4.5%)	49 (11.7%)	7.2%	2.6	26 (6.2%)	1.7%	1.4	31 (7.4%)	2.9%	1.6

		well-child visits at medical or pediatric clinics													
Gräfe, 2004[g,47]	Germany	Medical and psychosomatic outpatients	494	42 (14)	331 (67%)	67 (13.6%)	166 (33.6%)	20.0%	2.5	97 (19.6%)	6.1%	1.4	86 (17.4%)	3.8%	1.3
Green, 2017[48]	USA	Returning veterans	176	37 (10)	95 (54%)	22 (12.5%)	65 (36.9%)	24.4%	3.0	31 (17.6%)	5.1%	1.4	32 (18.2%)	5.7%	1.5
Green, 2018[49]	Kenya	Pregnant women and new mothers	192	27 (6)	192 (100%)	10 (5.2%)	100 (52.1%)	46.9%	10.0	67 (34.9%)	29.7%	6.7	62 (32.3%)	27.1%	6.2
Haroz, 2017[50]	Myanmar	Primary care patients	132	48 (14)	86 (65%)	29 (22.0%)	25 (18.9%)	-3.0%	0.9	16 (12.1%)	-9.8%	0.6	13 (9.8%)	-12.1%	0.4
Hitchon, 2019[h,51]	Canada	Rheumatoid arthritis patients	148	61 (12)	124 (84%)	16 (10.8%)	44 (29.7%)	18.9%	2.8	22 (14.9%)	4.1%	1.4	26 (17.6%)	6.8%	1.6
Khamseh, 2011[d,i,52]	Iran	Type 2 diabetes patients	184	56 (9)	96 (52%)	79 (42.9%)	103 (56%)	13.0%	1.3	81 (44.0%)	1.1%	1.0	55 (45.1%)	6.6%	1.2
Kwan, 2012[53]	Singapore	Post-stroke in-patients undergoing rehabilitation	113	60 (12)	37 (33%)	3 (2.7%)	24 (21.2%)	18.6%	8.0	9 (8.0%)	5.3%	3.0	7 (6.2%)	3.5%	2.3
Lambert, 2015[54]	Australia	Cancer patients	147	58 (10)	96 (65%)	21 (14.3%)	38 (25.9%)	11.6%	1.8	21 (14.3%)	0.0%	1.0	18 (12.2%)	-2.0%	0.9
Lara, 2015[55]	Mexico	Pregnant women during the third trimester of pregnancy	280	29 (6)	280 (100%)	29 (10.4%)	57 (20.4%)	10.0%	2.0	21 (7.5%)	-2.9%	0.7	23 (8.2%)	-2.1%	0.8
Marrie, 2018[56]	Canada	Multiple sclerosis patients	244	53 (13)	198 (81%)	25 (10.2%)	73 (29.9%)	19.7%	2.9	43 (17.6%)	7.4%	1.7	36 (14.8%)	4.5%	1.4
Martin-Subero, 2017[57]	Spain	Medical in-patients	1003	43 (14)	457 (46%)	83 (8.3%)	289 (28.8%)	20.5%	3.5	154 (15.4%)	7.1%	1.9	143 (14.3%)	6.0%	1.7
Osório, 2009[58]	Brazil	Women in primary care	177	33 (7)	177 (100%)	60 (33.9%)	62 (35%)	1.1%	1.0	45 (25.4%)	-8.5%	0.8	43 (24.3%)	-9.6%	0.7
Osório, 2012[59]	Brazil	Inpatients from various clinical wards	86	49 (12)	35 (41%)	28 (32.6%)	41 (47.7%)	15.1%	1.5	26 (30.2%)	-2.3%	0.9	26 (30.2%)	-2.3%	0.9
Patten, 2015[60]	Canada	Multiple sclerosis patients	143	50 (12)	110 (77%)	20 (14.0%)	36 (25.2%)	11.2%	1.8	24 (16.8%)	2.8%	1.2	12 (8.4%)	-5.6%	0.6
Picardi, 2005[61]	Italy	Inpatients with skin diseases	138	37 (13)	77 (56%)	12 (8.7%)	38 (27.5%)	18.8%	3.2	21 (15.2%)	6.5%	1.8	18 (13.0%)	4.3%	1.5
Prisnie, 2016[62]	Canada	Stroke and transient ischemic attach patients	114	60 (16)	64 (56%)	11 (9.6%)	16 (14%)	4.4%	1.5	11 (9.6%)	0.0%	1.0	9 (7.9%)	-1.8%	0.8
Quinn, Unpublished[h,j]	UK	Stroke patients	146	68 (13)	65 (47%)	17 (11.6%)	43 (29.5%)	17.8%	2.5	17 (11.6%)	0.0%	1.0	17 (12.6%)	1.5%	1.1
Richardson, 2010[63]	USA	Older adults undergoing in-home aging services care management assessment	377	77 (9)	258 (68%)	95 (25.2%)	117 (31%)	5.8%	1.2	65 (17.2%)	-8.0%	0.7	60 (15.9%)	-9.3%	0.6
Rooney, 2013[64]	UK	Adults with cerebral glioma	126	54 (12)	54 (43%)	14 (11.1%)	27 (21.4%)	10.3%	1.9	15 (11.9%)	0.8%	1.1	13 (10.3%)	-0.8%	0.9

Shinn, 2017[k,65]	USA	Cancer patients	139	59 (11)	139 (100%)	12 (8.6%)	24 (17.3%)	8.6%	2.0	11 (7.9%)	-0.7%	0.9	8 (6.5%)	2.4%	1.6
Sidebottom, 2012[l,66]	USA	Pregnant women	246	25 (5)	246 (100%)	12 (4.9%)	59 (24%)	19.1%	4.9	32 (13.0%)	8.1%	2.7	32 (13.0%)	8.1%	2.7
Simning, 2012[67]	USA	Older adults living in public housing	190	68 (7)	110 (58%)	10 (5.3%)	25 (13.2%)	7.9%	2.5	11 (5.8%)	0.5%	1.1	9 (4.7%)	-0.5%	0.9
Spangenberg, 2015[68]	Germany	Primary care patients	160	72 (6)	97 (61%)	1 (0.6%)	9 (5.6%)	5.0%	9.0	4 (2.5%)	1.9%	4.0	4 (2.5%)	1.9%	4.0
Turner, 2012[69]	Australia	Stroke patients	72	67 (13)	34 (47%)	13 (18.1%)	22 (30.6%)	12.5%	1.7	12 (16.7%)	-1.4%	0.9	9 (12.5%)	-5.6%	0.7
Turner, Unpublished[h]	Australia	Cardiac rehabilitation patients	51	60 (12)	7 (14%)	4 (7.8%)	6 (11.8%)	3.9%	1.5	2 (3.9%)	-3.9%	0.5	2 (3.9%)	-3.9%	0.5
Vöhringer, 2013[a,33]	Chile	Primary care patients	190	50 (17)	143 (75%)	59 (31.1%)	85 (44.7%)	13.7%	1.4	54 (28.4%)	-2.6%	0.9	--	--	--
Wagner, 2017[b,70]	USA	Patients starting radiotherapy for the first diagnosis of any tumor	54	59 (11)	38 (69%)	6 (4.3%)	13 (5.3%)	0.9%	1.2	7 (2.8%)	-1.5%	0.7	6 (2.4%)	-1.9%	0.6
Williams, 2012[71]	USA	Parkinson's Disease patients	235	66 (10)	76 (32%)	61 (26.0%)	47 (20.0%)	-6.0%	0.8	17 (7.2%)	-18.7%	0.3	17 (7.2%)	-18.7%	0.3
Wittkampf, 2009[b,72]	Netherlands	Primary care patients at risk for depression	260	51 (12)	175 (64%)	45 (11.6%)	90 (22.2%)	10.6%	1.9	49 (11.6%)	0.0%	1.0	44 (10.4%)	-1.2%	0.9
Studies from IPDMA that used other Semi-structured Interviews and were Included in Sensitivity Analyses															
Liu, 2011[m,73]	Taiwan	Primary care patients	1532	53 (19)	933 (61%)	50 (3.3%)	133 (8.7%)	5.4%	2.7	46 (3.0%)	-0.3%	0.9	50 (3.3%)	0.0%	1.0
McGuire, 2013[n,74]	USA	Acute coronary syndrome inpatients	100	63 (12)	31 (31%)	9 (9.0%)	25 (25.0%)	16.0%	2.8	13 (13.0%)	4.0%	1.4	12 (12.0%)	3.0%	1.3
Twist, 2013[b,c,m,o,75]	UK	Type 2 diabetes outpatients	360	56 (11)	172 (45%)	80 (7.4%)	178 (14.8%)	7.4%	2.0	112 (9.3%)	1.9%	1.3	97 (8.2%)	0.7%	1.1

[a]Study did not provide item-level data necessary to determine classification based on the PHQ-9 diagnostic algorithm
[b]Sampling weights were applied. Counts are based on actual numbers, whereas percentages are weighted
[c]1 participant missing data for age
[d]10 participants missing data for age
[e]1 participant missing data for both age and sex
[f]2 participants missing data for age
[g]21 participants missing data for age
[h]Unpublished at the time of electronic database search
[i]62 participants missing data to determine classification based on the PHQ-9 diagnostic algorithm
[j]2 participants missing data for age, 7 participants missing data for sex, 10 participants missing data to determine classification based on the PHQ-9 diagnostic algorithm, and 1 participant missing data for age, sex and diagnostic algorithm
[k]2 participants missing data for age, 14 participants missing data to determine classification based on the PHQ-9 diagnostic algorithm, and 1 participant missing data for age and diagnostic algorithm
[l]4 participants missing data for age
[m]Diagnostic interview: Schedules for Clinical Assessment in Neuropsychiatry
[n]Diagnostic interview: Depression Interview and Structured Hamilton
[o]8 participants missing data to determine classification based on the PHQ-9 diagnostic algorithm
Abbreviations: DA+: positive classification based on PHQ-9 diagnostic algorithm

FIGURE LEGENDS

Figure 1. Flow diagram of study selection process